Affiliated Genetics
2749 East Parleys Way, Suite 100
Salt Lake City, UT 84109
CLIA ID: 46D1077919

Affiliated Pharmarisk Pain Created for

Patient:
HIPAA Compliant Fax:
Physician:
Address:
Collection Date:
Specimen Type:

Accession #:
Gender:
DOB:
Received Date:
Report Generated:

Key Test Findings

Pharmacogenetic Results

	Assay	Results	Phenotype	Clinical Consequences
⚠	ANKK1/DRD2	DRD2:Taq1A AG	Altered DRD2 function	Consistent with a reduced dopamine receptor D2 function.
⚠	COMT	Val158Met AA	Low COMT Activity	Consistent with a significantly reduced catechol O-methyltransferase (COMT) function.
✓	CYP1A2	*1F/*1L	Normal Metabolizer- Possible Inducibility	Consistent with a typical CYP1A2 activity in absence of inducing substances. Rapid metabolism may occur in presence of inducers such as barbiturates, cruciferous vegetables, carbamazepine, rifampin and smoking.
⚠	CYP2B6	*1/*9	Intermediate Metabolizer	Consistent with a moderate deficiency in CYP2B6 activity. Potential risk for side effects or loss of efficacy with drug substrates.
🚩	CYP2C19	*1/*17	Rapid Metabolizer	Consistent with a significant increase in CYP2C19 activity. Potential risk for side effects or loss of efficacy with drug substrates.
✓	CYP2C9	*1/*1	Normal Metabolizer	Consistent with a typical CYP2C9 activity. This test did not identify risks for side effects or loss of efficacy with drug substrates.
🚩	CYP2D6	*2/*41 XN	Rapid or Normal Metabolizer	Consistent with typical or increased CYP2D6 activity. Potential risk for side effects or loss of efficacy with drug substrates.
✓	CYP3A4	*1/*1	Normal Metabolizer	Consistent with a typical CYP3A4 activity. Caution is advised when prescribing narrow therapeutic index drugs. Alternative drugs or dose adjustment may be required if CYP3A inhibitors or inducers are co-prescribed.
✓	CYP3A5	*3/*3	Poor Metabolizer	Consistent with a poor CYP3A5 activity. Caution is advised when prescribing narrow therapeutic index drugs. Alternative drugs or dose adjustment may be required if CYP3A inhibitors or inducers are co-prescribed.
⚠	OPRM1	A118G AG	Altered OPRM1 Function	Consistent with a reduced OPRM1 receptor signaling efficiency induced by exogenous opioids. This is associated with a possible reduced analgesia following standard opioid doses and a favorable response to naltrexone.
⚠	UGT2B15	*1/*2	Intermediate Metabolizer	Consistent with a moderately decreased UGT2B15 glucuronidation function. Potential risk for side effects with drug substrates.

Medication Guidance

Psychotropic Medications

Standard Precautions	Use With Caution	Consider Alternatives
Aripiprazole (Abilify)	Amphetamine (Adderall)	Amitriptyline (Elavil)
Clobazam (Onfi)	Bupropion (Wellbutrin)	Atomoxetine (Strattera)
Desvenlafaxine (Pristiq)	Clozapine (Clozaril)	Citalopram (Celexa)
Duloxetine (Cymbalta)	Dexmethylphenidate (Focalin)	Clomipramine (Anafranil)
Gabapentin (Neurontin)	Dextroamphetamine (Dexedrine)	Desipramine (Norpramin)
Galantamine (Razadyne)	Diazepam (Valium)	Doxepin (Silenor)
Iloperidone (Fanapt)	Donepezil (Aricept)	Escitalopram (Lexapro)
Mirtazapine (Remeron)	Lisdexamfetamine (Vyvanse)	Haloperidol (Haldol)
Naltrexone (Vivitrol)	Lorazepam (Ativan)	Imipramine (Tofranil)
Paliperidone (Invega)	Methylphenidate (Ritalin)	Nortriptyline (Pamelor)
Phenytoin (Dilantin)	Olanzapine (Zyprexa)	Paroxetine (Paxil)
Pregabalin (Lyrica)	Oxazepam (Serax)	Risperidone (Risperdal)
Sertraline (Zoloft)	Perphenazine (Trilafon)	Trimipramine (Surmontil)
Thioridazine (Mellaril)	Pimozide (Orap)	Venlafaxine (Effexor)
Vortioxetine (Brintellix)	Tetrabenazine (Xenazine)	

Cardiovascular Medications

Standard Precautions	Use With Caution	Consider Alternatives
Carvedilol (Coreg)	Atorvastatin (Lipitor)	Flecainide (Tambocor)
Fluvastatin (Lescol)	Clopidogrel (Plavix)	Metoprolol (Lopressor)
Irbesartan (Avapro)	Mexiletine (Mexitil)	Simvastatin (Zocor)
Lovastatin (Mevacor)	Pitavastatin (Livalo)	
Nebivolol (Bystolic)	Pravastatin (Pravachol)	
Prasugrel (Effient)	Propafenone (Rythmol)	
Propranolol (Inderal)	Rosuvastatin (Crestor)	
Ticagrelor (Brilinta)		
Timolol (Timoptic)		
Warfarin (Coumadin)		

Pain Medications

Standard Precautions	Use With Caution	Consider Alternatives
Buprenorphine (Butrans, Buprenex)	Carisoprodol (Soma)	Codeine (Codeine)
Celecoxib (Celebrex)	Dihydrocodeine (Synalgos-DC)	Tramadol (Ultram)
Cyclobenzaprine (Flexeril, Amrix)	Fentanyl (Actiq)	
Flurbiprofen (Ansaid)	Hydrocodone (Vicodin)	
Hydromorphone (Dilaudid, Exalgo)	Methadone (Dolophine)	
Meperidine (Demerol)	Morphine (MS Contin)	
Oxymorphone (Opana, Numorphan)	Oxycodone (Percocet)	
Piroxicam (Feldene)	Tizanidine (Zanaflex)	
Tapentadol (Nucynta)		

Other Medications

Standard Precautions	Use With Caution	Consider Alternatives
Darifenacin (Enablex)	Dexlansoprazole (Dexilant)	Ondansetron (Zofran)
Fesoterodine (Toviaz)	Esomeprazole (Nexium)	
Glimepiride (Amaryl)	Lansoprazole (Prevacid)	
Glipizide (Glucotrol)	Omeprazole (Prilosec)	
Glyburide (Micronase)	Pantoprazole (Protonix)	
Metoclopramide (Reglan)	Voriconazole (Vfend)	
Mirabegron (Myrbetriq)		
Rabeprazole (Aciphex)		
Tacrolimus (Prograf)		
Tamsulosin (Flomax)		
Tolbutamide (Orinase)		
Tolterodine (Detrol)		

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Test Details

Gene	Alleles Tested
ANKK1/DRD2	DRD2:Taq1A
COMT	Val158Met
CYP1A2	*1C, *1D, *1F, *1K, *1L, *1V, *1W
CYP2B6	*4, *5, *6, *8, *9, *11, *18, *22, *28
CYP2C19	*2, *3, *4, *4B, *5, *6, *7, *8, *9, *10, *12, *17
CYP2C9	*2, *3, *4, *5, *6, *8, *10, *11, *12, *15, *25, *27
CYP2D6	*2, *3, *4, *4M, *6, *7, *8, *10, *11, *12, *14A, *15, *17, *18, *19, *20, *29, *35, *38, *41, *44, *56, *5 (gene deletion), XN (gene duplication)
CYP3A4	*1B, *2, *3, *12, *17, *22
CYP3A5	*1D, *2, *3, *3C, *5, *6, *7, *8, *9
OPRM1	A118G
UGT2B15	*2

Methodology:

Testing is performed on DNA extracted from a buccal swab. Samples are genotyped using Taqman® allele discrimination assays. The assays detect alleles listed above, including all common and most rare variants with known clinical significance at analytical sensitivity and specificity >99%.

Limitations:

The interpretations provided in this report are provided to assist health care providers, but they are not a treatment recommendation. Diagnosis and treatment remain the sole responsibility of the ordering physician. While the polymorphisms tested are important, other variants and mutations in these genes will not be detected. Mutations in other genes that could affect drug metabolism will not be detected. Non-genetic factors also affect metabolism. This test is not a substitute for clinical and therapeutic drug monitoring. This report does not address patient drug allergies or drug-drug interactions.

Signature:

Kenneth Ward M.D.

Date: 4/14/2014

CLIA FDA Statement:

This Laboratory Developed Test was developed and its performance characteristics determined by Affiliated Genetic, Inc. The laboratory is regulated under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high-complexity clinical testing and has established and verified the test's accuracy. This test has not been cleared or approved by the U.S. Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary. These results are adjunctive to an ordering physician's diagnosis.

Appendix: Dosing Guidance

Amitriptyline (Elavil)

Increased Sensitivity to Amitriptyline (CYP2C19 *1/*17 Rapid Metabolizer)

Consider an alternative drug or consider prescribing amitriptyline at standard dose and monitor the plasma concentrations of amitriptyline and nortriptyline to guide dose adjustments.

Amitriptyline (Elavil)

Possible Non-Response to Amitriptyline (CYP2D6 *2/*41 XN Rapid or Normal Metabolizer)

Based on the genotype result, this patient MAY be a CYP2D6 rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 rapid metabolizers: consider alternative drug or prescribe amitriptyline at increased dose and monitor the plasma concentrations of amitryptyline and metabolites (there is insufficient data to calculate dose adjustment). Available alternative drugs not sensitive to CYP2D6 function include: sertraline, citalopram, escitalopram and fluvoxamine.

Amphetamine (Adderall)

Poor Response to Amphetamine salts (COMT Val158Met AA Low COMT Activity)

The patient's genotype predicts a reduced therapeutic response to amphetamine stimulants. If prescribed, amphetamines should be administered at the lowest effective dose and dosage should be individually adjusted.

Atomoxetine (Strattera)

Possible Non-Response to Atomoxetine (CYP2D6 *2/*41 XN Rapid or Normal Metabolizer)

Based on the genotype result, this patient MAY be a CYP2D6 rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 rapid metabolizers: consider prescribing atomoxetine with careful titration and monitoring for reduced efficacy. There is insufficient data to calculate dose adjustment. Or consider alternative drug such as methylphenidate.

Atorvastatin (Lipitor)

Increased Myopathy Risk (SLCO1B1 521T>C TC Intermediate Transporter Function)

The reduced SLCO1B1 function may result in elevated atorvastatin plasma levels. Because the risk of myopathy increases in patients with high statin plasma levels, the use of high atorvastatin doses in this patient should be avoided. If atorvastatin is used in this patient, a closer monitoring of serum creatine kinase and liver function is recommended. Other myopathy predisposing factors include advanced age (≥65), uncontrolled hypothyroidism, renal impairment, comedications and female gender.

Bupropion (Wellbutrin)

Decreased Response to Bupropion (ANKK1 DRD2:Taq1A AG Altered DRD2 function)

Smoking Cessation: The patient's genotype is associated with a positive response to nicotine replacement therapy and a lesser response to bupropion treatment.

Carisoprodol (Soma)

Altered Sensitivity to Carisoprodol (CYP2C19 *1/*17 Rapid Metabolizer)

There is insufficient data to allow calculation of dose adjustment and if carisodoprol is prescribed, it is recommended to use a lower dose and to carefully monitor the patient for side effects.

Citalopram (Celexa)

Insufficient Response to Citalopram (CYP2C19 *1/*17 Rapid Metabolizer)

The patient may not respond to usual doses. Monitor plasma concentration and increase dose to a maximum of 150% in response to efficacy and adverse events or select alternative drug.

Clomipramine (Anafranil)

Increased Sensitivity to Clomipramine (CYP2C19 *1/*17 Rapid Metabolizer)

Consider an alternative drug or consider prescribing clomipramine at standard dose and monitor the plasma concentrations of clomipramine and desmethyl-clomipramine to guide dose adjustments.

Clomipramine (Anafranil)

Possible Non-Response to Clomipramine (CYP2D6 *2/*41 XN Rapid or Normal Metabolizer)

Based on the genotype result, this patient MAY be a CYP2D6 rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 rapid metabolizers: consider alternative drug or prescribe clomipramine at increased dose and monitor the plasma concentrations of clomipramine and desmethylclomipramine. Available alternative drugs not sensitive to CYP2D6 function include: sertraline, citalopram, escitalopram and fluvoxamine.

Clopidogrel (Plavix)

Increased Response to Clopidogrel (CYP2C19 *1/*17 Rapid Metabolizer)

Clopidogrel can be prescribed at standard label-recommended dosage. Individuals with the *17 allele may have an increased risk of bleeding while taking clopidogrel.

Clozapine (Clozaril)

Possible Non-Response to Clozapine (CYP1A2 *1F/*1L Normal Metabolizer- Possible Inducibility)

Smokers may be at risk for non-response and may require higher doses. There is an association between high clozapine doses and the risk of seizures, therefore careful monitoring is recommended during dosing adjustment. Smoking cessation may increase plasma drug levels leading to adverse events and therapeutic drug monitoring accompanied by dose reduction is recommended in patients who have quit smoking.

Codeine (Codeine)

Possible Increased Response to Codeine (CYP2D6 *2/*41 XN Rapid or Normal Metabolizer)

Based on the genotype result, this patient MAY be a CYP2D6 rapid metabolizer. Greatly increased morphine levels are expected and the patient is at high risk of toxicity when taking codeine. Avoid prescribing codeine and consider an alternative opioid or consider a non-opioid analgesic such as a NSAID or a COX-2 inhibitor. Unless contraindicated, available alternative opioids not sensitive to CYP2D6 function include: Fentanyl, Morphine, Hydromorphone, Oxymorphone, Tapentadol and Meperidine.

Desipramine (Norpramin)

Possible Non-Response to Desipramine (CYP2D6 *2/*41 XN Rapid or Normal Metabolizer)

Based on the genotype result, this patient MAY be a CYP2D6 rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 rapid metabolizers: consider alternative drug or prescribe desipramine at increased dosage and observe the patient for decreased efficacy. Adjust dosage in response to desipramine and metabolites plasma concentrations and clinical response.

Dexlansoprazole (Dexilant)

Possible Insufficient Response to Dexlansoprazole (CYP2C19 *1/*17 Rapid Metabolizer)

Be alert to insufficient response and **consider dose increase**. There is insufficient data to allow calculation of dose adjustment.

Dexmethylphenidate (Focalin)

Poor Response to Dexmethylphenidate (COMT Val158Met AA Low COMT Activity)

The patient's genotype predicts a reduced therapeutic response to dexmethylphenidate. Dosage should be individualized according to the needs and responses of the patient. Therapy should be initiated in small doses, with gradual weekly increments.

Dextroamphetamine (Dexedrine)

Poor Response to Dextroamphetamine (COMT Val158Met AA Low COMT Activity)

The patient's genotype predicts a reduced therapeutic response to amphetamine stimulants. If prescribed, dextroamphetamine should be administered at the lowest effective dose and dosage should be individually adjusted.

Diazepam (Valium)

Altered Sensitivity to Diazepam (CYP2C19 *1/*17 Rapid Metabolizer)

There is insufficient data to allow calculation of dose adjustment when diazepam is prescribed. Monitor the response and adjust the dose accordingly or select an alternative drug.

Dihydrocodeine (Synalgos-DC)

Possible Altered Response to Dihydrocodeine (CYP2D6 *2/*41 XN Rapid or Normal Metabolizer)

Increased conversion of dihydrocodeine to the more active metabolite dihydromorphine is expected in CYP2D6 rapid metabolizers. This may result in an exaggerated response. Adequate pain relief can be achieved by decreasing the dose in response to pain symptoms. Other opioids not metabolized by CYP2D6 (i.e. morphine, oxymorphone, buprenorphine, fentanyl, methadone and hydromorphone) may also be considered if signs of overdose (excessive sleepiness, confusion, or shallow breathing) are reported.

Donepezil (Aricept)

Possible Altered Response to Donepezil (CYP2D6 *2/*41 XN Rapid or Normal Metabolizer)

Based on the genotype result, this patient MAY be a CYP2D6 rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 rapid metabolizers: when compared to a normal metabolizer, a rapid metabolizers has a 24% increase in donepezil clearance; the clinical significance of this increase is not well documented. Consider using a standard dosing regimen and adjust dosage in response to clinical response and tolerability.

Doxepin (Silenor)

Increased Sensitivity to Doxepin (CYP2C19 *1/*17 Rapid Metabolizer)

Consider an alternative drug or consider prescribing doxepin at standard dose and monitor the plasma concentrations of doxepin and desmethyl-doxepin to guide dose adjustments.

Doxepin (Silenor)

Possible Non-Response to Doxepin (CYP2D6 *2/*41 XN Rapid or Normal Metabolizer)

Based on the genotype result, this patient MAY be a CYP2D6 rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 rapid metabolizers: consider alternative drug or increase doxepin dose by 100%. Adjust maintenance dose according to nordoxepin plasma concentrations. Available alternative drugs not sensitive to CYP2D6 function include: sertraline, citalopram, escitalopram and fluvoxamine.

Escitalopram (Lexapro)

Insufficient Reponse to Escitalopram (CYP2C19 *1/*17 Rapid Metabolizer)

Monitor plasma concentration and titrate dose to a maximum of 150% in response to efficacy and adverse events or select alternative drug.

Esomeprazole (Nexium)

Insufficient Response to Esomeprazole (CYP2C19 *1/*17 Rapid Metabolizer)

- Helicobacter pilori eradication: increase dose by 50-100% and be alert to insufficient response.
- Other: be extra alert to insufficient response and consider dose increase by 50-100%.

Fentanyl (Actiq)

Altered Response to Fentanyl (OPRM1 A118G AG Altered OPRM1 Function)

Acute postoperative and cancer pain: the patient's genotype has been shown to be associated with reduced analgesia at standard fentanyl doses. Therefore the patient may require higher doses of this drug. Because fentanyl has a narrow therapeutic window, it is advised to carefully titrate this drug to a tolerable dose that provides adequate analgesia with minimal side effects.

Flecainide (Tambocor)

Altered Response to Flecainide (CYP2D6 *2/*41 XN Rapid or Normal Metabolizer)

Based on the genotype result, this patient MAY be a CYP2D6 rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 rapid metabolizers: titrate carefully and consider adjusting dose in response to plasma concentration and ECG monitoring OR consider alternative drug. Example of alternatives drugs not affected by CYP2D6 include: sotalol, disopyramide, quinidine and amiodarone.

Haloperidol (Haldol)

Possible Non-Response to Haloperidol (CYP2D6 *2/*41 XN Rapid or Normal Metabolizer)

Based on the genotype result, this patient MAY be a CYP2D6 rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 rapid metabolizers: consider alternative drug or prescribe haloperidol at standard dose and adjust dosage to achieve a favorable clinical response. Be alert to decreased haloperidol plasma concentrations. Available alternative drugs include: pimozide; fluphenazine, quetiapine, olanzapine and clozapine.

Hydrocodone (Vicodin)

Possible Altered Response to Hydrocodone (CYP2D6 *2/*41 XN Rapid or Normal Metabolizer)

Based on the genotype result, this patient MAY be a CYP2D6 rapid metabolizer. Increased conversion of hydrocodone to the more active metabolite hydromorphone is expected in CYP2D6 rapid metabolizers. Usually, adequate pain relief without an increase in adverse events can be achieved by using standard or lower hydrocodone doses. Other opioids not metabolized by CYP2D6 (i.e. morphine, oxymorphone, buprenorphine, fentanyl, methadone and hydromorphone) may also be considered if excessive side effects are reported.

Hydrocodone (Vicodin)

Altered Response to Hydrocodone (OPRM1 A118G AG Altered OPRM1 Function)

Acute postoperative and cancer pain: the patient's genotype has been shown to be associated with reduced analgesia and increased opioid side effects at standard or high hydrocodone doses. If the patient fails to respond to increased hydrocodone doses, an alternative opioid may be considered.

Imipramine (Tofranil)

Increased Sensitivity to Imipramine (CYP2C19 *1/*17 Rapid Metabolizer)

Consider an alternative drug or consider prescribing imipramine at standard dose and monitor the plasma concentrations of imipramine and desipramine to guide dose adjustments.

Imipramine (Tofranil)

Possible Non-Response to Imipramine (CYP2D6 *2/*41 XN Rapid or Normal Metabolizer)

Based on the genotype result, this patient MAY be a CYP2D6 rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 rapid metabolizers: consider alternative drug or consider increasing imipramine dose and adjust dosage in response to imipramine and desipramine plasma concentrations. Available alternative drugs not sensitive to CYP2D6 function include: sertraline, citalopram, escitalopram and fluvoxamine.

Lansoprazole (Prevacid)

Insufficient Response to Lansoprazole (CYP2C19 *1/*17 Rapid Metabolizer)

- Helicobacter pilori eradication: increase dose by 200% and be alert to insufficient response.
- Other: be extra alert to insufficient response and consider dose increase by 200%.

Lisdexamfetamine (Vyvanse)

Poor Response to Lisdexamfetamine (COMT Val158Met AA Low COMT Activity)

The patient's genotype predicts a reduced therapeutic response to amphetamine stimulants. If prescribed, lisdexamfetamine should be administered at the lowest effective dose and dosage should be individually adjusted.

Lorazepam (Ativan)

Possible Altered Response to Lorazepam (UGT2B15 *1/*2 Intermediate Metabolizer)

Lorazepam clearance may be reduced in this patient. However, there is insufficient evidence as to whether this change results in a significant clinical effect. Consider monitoring the patient for increased sedation and adjust dosing accordingly.

Methadone (Dolophine)

Possible Sensitivity to Methadone (CYP2B6 *1/*9 Intermediate Metabolizer)

Consider lower starting doses of methadone and adust dosing based on the clinical response.

Methylphenidate (Ritalin)

Poor Response to Methylphenidate (COMT Val158Met AA Low COMT Activity)

The patient's genotype predicts a reduced therapeutic response to methylphenidate. Dosage should be individualized according to the needs and responses of the patient. Therapy should be initiated in small doses, with gradual weekly increments.

Metoprolol (Lopressor)

Possible Non-Responder to Metoprolol (CYP2D6 *2/*41 XN Rapid or Normal Metabolizer)

Based on the genotype result, this patient MAY be a CYP2D6 rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 rapid metabolizers: the patient may experience a decrease in the pharmacological effect when taking metoprolol at standard dosage. Heart Failure: Consider alternative beta-blockers such as bisoprolol or carvedilol or prescribe metoprolol at a higher dose. Other indications: Consider alternative beta-blockers such as bisoprolol or atenolol or or prescribe metoprolol at a higher dose. If metoprolol is prescribed, titrate dose to a maximum of 250% of the normal dose in response to efficacy and adverse events.

Mexiletine (Mexitil)

Altered Response to Mexiletine (CYP2D6 *2/*41 XN Rapid or Normal Metabolizer)

Based on the genotype result, this patient MAY be a CYP2D6 rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 rapid metabolizers: because mexiletine plasma concentrations may be decreased, consider adjusting dose in response to mexiletine plasma concentration and ECG monitoring until a favorable response in achieved.

Morphine (MS Contin)

Altered Response to Morphine (COMT Val158Met AA Low COMT Activity)

The patient may require lower doses of morphine for adequate pain control. Dosing regimen needs to be individualized for each patient, taking into account the patient's prior analgesic treatment experience. Monitor the patient closely for respiratory depression, especially within the first 24-72 hours of initiating therapy.

Nortriptyline (Pamelor)

Possible Non-Response to Nortriptyline (CYP2D6 *2/*41 XN Rapid or Normal Metabolizer)

Based on the genotype result, this patient MAY be a CYP2D6 rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 rapid metabolizers: consider alternative drug or prescribe nortriptyline at increased dose and monitor the plasma concentration of nortriptyline and hydroxynortriptyline. Available alternative drugs not sensitive to CYP2D6 function include: sertraline, citalopram, escitalopram and fluvoxamine.

Olanzapine (Zyprexa)

Possible Non-Response to Olanzapine (CYP1A2 *1F/*1L Normal Metabolizer- Possible Inducibility)

There is little evidence regarding the impact of CYP1A2 genetic variants on olanzapine response. Smokers may be at risk for non-response at standard doses. Careful monitoring is recommended during dosing adjustment. Smoking cessation may increase plasma drug levels leading to adverse events and therapeutic drug monitoring accompanied by dose reduction may be needed in patients who have quit smoking.

Omeprazole (Prilosec)

Insufficient Response to Omeprazole (CYP2C19 *1/*17 Rapid Metabolizer)

- Helicobacter pilori eradication: increase dose by 100-200% and be alert to insufficient response.
- Other: be extra alert to insufficient response and consider dose increase by 100-200%.

Ondansetron (Zofran)

Possible Non-Response to Ondansetron (CYP2D6 *2/*41 XN Rapid or Normal Metabolizer)

Based on the genotype result, this patient MAY be a CYP2D6 rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 rapid metabolizers: a substantially decreased antiemetic effect has been reported in these patients. Consider prescribing an alternative drug not metabolized by CYP2D6 such as granisetron.

Oxazepam (Serax)

Possible Altered Response to Oxazepam (UGT2B15 *1/*2 Intermediate Metabolizer)

Oxazepam clearance may be reduced in this patient. However, there is insufficient evidence as to whether this change results in a significant clinical effect. Consider monitoring the patient for increased sedation and adjust dosing accordingly.

Oxycodone (Percocet)

Possible Altered Response to Oxycodone (CYP2D6 *2/*41 XN Rapid or Normal Metabolizer)

Based on the genotype result, this patient MAY be a CYP2D6 rapid metabolizer. Increased conversion of oxycodone to the more active metabolite oxymorphone is expected in CYP2D6 rapid metabolizers. Usually, adequate pain relief without an increase in adverse events can be achieved by using standard or lower oxycodone doses. Other opioids not metabolized by CYP2D6 (i.e. morphine, oxymorphone, buprenorphine, fentanyl, methadone and hydromorphone) may also be considered if excessive side effects are reported.

Pantoprazole (Protonix)

Insufficient Response to Pantoprazole (CYP2C19 *1/*17 Rapid Metabolizer)

- Helicobacter pilori eradication: increase dose by 400% and be alert to insufficient response.
- Other: be extra alert to insufficient response and consider dose increase by 400%.

Paroxetine (Paxil)

Possible Non-Response to Paroxetine (CYP2D6 *2/*41 XN Rapid or Normal Metabolizer)

Based on the genotype result, this patient MAY be a CYP2D6 rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 rapid metabolizers: consider alternative drug or increase paroxetine dose and adjust dosage in response to efficacy. Available alternative drugs not sensitive to CYP2D6 function include: sertraline, citalopram, escitalopram and fluvoxamine.

Perphenazine (Trilafon)

Possible Non-Response to Perphenazine (CYP2D6 *2/*41 XN Rapid or Normal Metabolizer)

Based on the genotype result, this patient MAY be a CYP2D6 rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 rapid metabolizers: subjects with increased CYP2D6 function will metabolize perphenazine more rapidly which can result in sub-therapeutic drug concentrations. Consider a dose increase with close monitoring until a favorable response is achieved.

Pimozide (Orap)

Possible Non-Response to Pimozide (CYP2D6 *2/*41 XN Rapid or Normal Metabolizer)

Based on the genotype result, this patient MAY be a CYP2D6 rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 rapid metabolizers: there is insufficient data to calculate dose adjustment and if pimozide is prescribed at standard dosing, monitor response and be alert to reduced efficacy. Standard starting dose: 1 to 2 mg/day (adult) or 0.05 mg/kg/day (children) - Doses may be increased to a maximum of 10 mg/day or 0.2 mg/kg/day.

Pitavastatin (Livalo)

Increased Myopathy Risk (SLCO1B1 521T>C TC Intermediate Transporter Function)

The reduced SLCO1B1 function may result in elevated pitavastatin plasma levels. Because the risk of myopathy increases in patients with high statin plasma levels, the use of high pitavastatin doses in this patient should be avoided. If pitavastatin is used in this patient, a closer monitoring of serum creatine kinase and liver function is recommended. Other myopathy predisposing factors include advanced age (≥65), uncontrolled hypothyroidism, renal impairment, comedications and female gender.

Pravastatin (Pravachol)

Increased Myopathy Risk (SLCO1B1 521T>C TC Intermediate Transporter Function)

The reduced SLCO1B1 function may result in elevated pravastatin plasma levels. Because the risk of myopathy increases in patients with high statin plasma levels, the use of high pravastatin doses in this patient should be avoided. If pravastatin is used in this patient, a closer monitoring of serum creatine kinase and liver function is recommended. Other myopathy predisposing factors include advanced age (≥65), uncontrolled hypothyroidism, renal impairment, comedications and female gender.

Propafenone (Rythmol)

Altered Response to Propafenone (CYP2D6 *2/*41 XN Rapid or Normal Metabolizer)

Based on the genotype result, this patient MAY be a CYP2D6 rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 rapid metabolizers:titrate carefully and consider adjusting dose in response to plasma concentration and ECG monitoring OR consider alternative drug. Example of alternatives drugs not affected by CYP2D6 include: sotalol, disopyramide, quinidine and amiodarone.

Risperidone (Risperdal)

Possible Non-Response to Risperidone (CYP2D6 *2/*41 XN Rapid or Normal Metabolizer)

Based on the genotype result, this patient MAY be a CYP2D6 rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 rapid metabolizers: consider alternative drug; available alternative drugs include: quetiapine, olanzapine, clozapine. Or prescribe risperidone and be extra alert to insufficient response and adjust dosage in response to clinical response and adverse events.

Rosuvastatin (Crestor)

Increased Myopathy Risk (SLCO1B1 521T>C TC ABCG2 421C>A CC)

The patient does not carry a polymorphism in the ABCG2 gene that is associated with a higher rosuvastatin plasma exposure. The patient carries a polymorphism in the SLCO1B1 gene that is associated with an increased risk of myopathy. Rosuvastatin plasma concentrations are expected to increase and the patient's risk of rosuvastatin-induced myopathy is elevated. Other factors that may increase this risk further include: uncontrolled hypothyroidism, renal impairment, diabetes and comedications with ABCG2 or SLCO1B1 inhibitors. Patient's age is 20-60 years; maximum recommended dose range to reduce the risk of high statin exposure: 20-40 mg/day (highest dose). Start with usual doses 10-20 mg/day. It is possible to increase dose to 40 mg/day in Non-Asian patients if no other risk factors are present and if patient is closely monitored for adverse events. Patient's age is >60 years; maximum recommended dose range to reduce the risk of high statin exposure: 20 mg/day. Start with usual doses 10-20 mg/day or 5 mg/day in Asian patients.

Simvastatin (Zocor)

Intermediate Myopathy Risk (SLCO1B1 521T>C TC Intermediate Transporter Function)

Simvastatin plasma concentrations are expected to be elevated. **1-Consider avoiding simvastatin** and prescribe an alternative statin or an other hypolipidemic drug or **2-**Consider prescribing simvastatin at a lower starting dose (20 mg/day). Routine Creatine Kinase (CK) monitoring is also advised. **The FDA recommends against the 80 mg daily dose**. Although the association between the SLCO1B1 521C>T variant and myopathy risk is not clearly established for other statins such as atorvastatin, pitavastatin, rosuvastatin and pravastatin, caution is advised if high doses of these statins are used in this patient. Fluvastatin plasma levels are not affected by the SLCO1B1 521C>T variant.

Tetrabenazine (Xenazine)

Unknown Sensitivity to Tetrabenazine (CYP2D6 *2/*41 XN Rapid or Normal Metabolizer)

Individualization of dose with careful weekly titration is required. The first week's starting dose is 12.5 mg daily; second week, 25 mg (12.5 mg twice daily); then slowly titrate at weekly intervals by 12.5 mg to a tolerated dose. **The maximum daily dose in CYP2D6 rapid metabolizers is not defined. The maximum daily dose in normal metabolizers is 100 mg with a maximum single dose of 37.5 mg.** If serious adverse events occur, titration should be stopped and the dose of tetrabenazine should be reduced. If the adverse event(s) do not resolve, consider withdrawal of tetrabenazine.

Tizanidine (Zanaflex)

Possible Non-Response to Tizanidine (CYP1A2 *1F/*1L Normal Metabolizer- Possible Inducibility)

There is little evidence regarding the impact of CYP1A2 genetic variants on tizanidine response. Smokers may be at risk for non-response and may require higher doses. There is an association between high tizanidine plasma concentrations and the risk of hypotension and excessive sedation, therefore careful monitoring is recommended during dosing adjustment. Smoking cessation may increase plasma drug levels leading to excessive hypotension and sedation. Careful monitoring accompanied by dose reduction may be needed in patients who have quit smoking.

Tramadol (Ultram)

Possible Increased Response to Tramadol (CYP2D6 *2/*41 XN Rapid or Normal Metabolizer)

Based on the genotype result, this patient MAY be a CYP2D6 rapid metabolizer and is at high risk of toxicity when taking tramadol at standard dosing. Consider reducing tramadol dose by 30%. Careful monitoring for side effects and weekly titration are recommended. If toxicity, consider alternative opioids other than codeine or consider a non-opioid analgesic such as a NSAID or a COX-2 inhibitor. Unless contraindicated, available alternative opioids (not sensitive to CYP2D6 function) include: Fentanyl, Morphine, Hydromorphone, Oxymorphone, Tapentadol and Meperidine.

Trimipramine (Surmontil)

Increased Sensitivity to Trimipramine (CYP2C19 *1/*17 Rapid Metabolizer)

Consider an alternative drug or consider prescribing trimipramine at standard dose and monitor the plasma concentrations of trimipramine and desmethy-ltrimipramine to guide dose adjustments.

Trimipramine (Surmontil)

Possible Non-Response to Trimipramine (CYP2D6 *2/*41 XN Rapid or Normal Metabolizer)

Based on the genotype result, this patient MAY be a CYP2D6 rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 rapid metabolizers: consider alternative drug or consider prescribing trimipramine at an increased dose and then adjust dosage in response to trimipramine plasma concentrations. Available alternative drugs not sensitive to CYP2D6 function include: sertraline, citalopram, escitalopram and fluvoxamine.

Venlafaxine (Effexor)

Possible Non-Response to Venlafaxine (CYP2D6 *2/*41 XN Rapid or Normal Metabolizer)

Based on the genotype result, this patient MAY be a CYP2D6 rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 rapid metabolizers: consider alternative drug; available alternative drugs include: citalopram and sertraline. Or, increase venlafaxine dose to a maximum of 150% of the normal dose and monitor venlafaxine and O-desmethylvenlafaxine plasma concentrations.

Voriconazole (Vfend)

Non-response to Voriconazole (CYP2C19 *1/*17 Rapid Metabolizer)

Voriconazole plasma concentrations may be low when standard dosage is used, increasing the risk of loss of response and effectiveness. Closely monitor voriconazole plasma concentrations and adjust the dose accordingly.

Affiliated Genetics

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Prescription Alert

DOB

This individual has been tested for gene variants that may affect medications prescribed.

GENE	RESULT
ANKK1	Altered DRD2 function
COMT	Low COMT Activity
CYP1A2	Normal Metabolizer- Possible Inducibility
CYP2B6	Intermediate Metabolizer
CYP2C19	Rapid Metabolizer
CYP2C9	Normal Metabolizer
CYP2D6	Rapid or Normal Metabolizer
CYP3A4	Normal Metabolizer
CYP3A5	Poor Metabolizer
OPRM1	Altered OPRM1 Function
UGT2B15	Intermediate Metabolizer

Healthcare Providers: For up-to-date information concerning the impact of these genetic tests on drug precribing by may consult the PharmGKB database:

www.pharmgkb.org

Note:This patient has also been tested for common variants in the Factor II, Factor V, MTHFR, and ApoE genes.These results are available on the patient's medical records.